JoS JOURNAL OF STROKE

Journal of Stroke 2016;18(1):1-1
http://dx.doi.org/10.5853/jos.2016.00038

Editorial

Moyamoya Disease, Still a Mysterious Disorder

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Moyamoya disease (MMD) is a chronic occlusive cerebrovascular disease characterized by progressive stenosis at the terminal portion of the internal carotid artery and an abnormal vascular network at the base of the brain. The etiology remains unknown, and the treatment is not satisfactory. In this issue of *Journal of Stroke*, important review papers on MMD are published. They showed that genetic variations of *RNF213* in the 17q25-ter region make it an important susceptibility gene, and that MMD is most common in East Asian countries such as Korea and Japan. These epidemiological characteristics may be attributed to the high prevalence of the susceptibility gene in this region. Other issues including recent advances in surgical and interventional therapy are also summarized.

However, MMD is still a mysterious disorder. MMD is diagnosed on the basis of imaging findings: bilateral (or unilateral) distal internal carotid artery occlusion and basal collaterals. However, simple middle cerebral artery stenosis may evolve into MMD over time, and intracranial atherosclerosis may angiographically mimic MMD. Although gene testing is useful in the differential diagnosis, questions remain. *RNF* gene polymorphism is found to be present in 1/4 of patients with non-MMD intracranial atherosclerosis in East Asia,[1] suggesting that it is not specific for MMD. In practice, when we encounter a patient with *RNF* gene variation and intracranial arterial disease that is not angiographically consistent with MMD, we are not sure whether this case is of atypical MMD or of atherosclerosis. Given the fact that *RNF* gene polymorphism is not uncommon in the Japanese and Koreans and only a few develop MMD, *RNF* may simply be a susceptibility gene, and the final clinical presentation, that is, MMD, intracranial atherosclerosis, or no vascular lesion, may depend on the nature of a secondary insult or perhaps other genetic variations. This is a puzzling issue, and a recent case report of combined pathology (both MMD and atherosclerosis)[2] has provided further confusion.

Reviews on this issue showed that MMD cases are also found in Western countries, and the prevalence is increasing worldwide. Are the characteristics of MMD in the East and West the same? Is the real incidence increasing or are we simply detecting more cases with advanced imaging tools? Other difficult questions are; why are there two peaks of age, around 10 years and at 30-45 years? Why are patients 20-30 years old relatively unaffected? Are antiplatelet agents useful for MMD patients? Is surgical revascularization therapy beneficial for patients presenting with hemorrhagic stroke? In patients with asymptomatic MMD, what is the risk of future stroke and what are the predictive factors? Is there any way to prevent the progression of the disease?

The reviews provide more questions than solutions, and it seems that the answers remain far off. However, we have to realize that polymorphism in *RNF 213* gene was completely unheard of until 10 years ago. Ten years from now, with continued research, we might be involved in clinical trials that examine ways to prevent the development of MMD in young individuals with a susceptible gene.

References

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The author has no financial conflicts of interest.